Synthesis and Function of Artificial Ion Channels Based on Thermoresponsive Amphiphilic Block Copolymers

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Ion channels are integral membrane proteins that regulate ion permeation across cell membranes. Recently, synthetic ion channels have gained attention for their potential as substitutes for natural ion channels and as anticancer agents. [1] However, conventional synthetic ion channels, typically small molecules, face several challenges, including rapid clearance through renal filtration when administered intravenously.[2] Additionally, their poor water solubility often necessitates the use of organic solvents for membrane incorporation, limiting their practical in vivo applications. Therefore, the development of novel artificial ion channels that differ from peptide- or supramolecular-based systems is urgently needed.

We have previously reported that amphiphilic polymers with poly(propylene oxide) (PPO) as the hydrophobic segment enable the permeation of small water-soluble molecules when incorporated into liposomes in aqueous solvents.[3] Despite the hydrophobic nature of PPO, the hydrophobic PPO layer retains a certain amount of water,[4] which enabling the permeation of water-soluble compounds. Based on this, we hypothesized that this structure could also allow ions to partition within the hydrophobic layer, thus functioning as an artificial ion channel.

In this study, we synthesized an amphiphilic block polymer (OGlu-*b*-$PPO_{2.5K}$) consisting of pegylated oligo(glutamic acid) as the hydrophilic segment and PPO as the hydrophobic segment to develop an artificial ion channel suitable for in vivo applications. The self-assembly behavior of OGlu-*b*-$PPO_{2.5K}$ was examined using transmission electron microscopy, and small-angle X-ray and neutron scattering, revealing the formation of spherical bilayer vesicles with 22.5 vol% water content in the PPO layer. The HPTS and potassium green assays demonstrated that the polymer, when incorporated into DOPC liposomes or cancer cells, facilitates ion permeation across membranes. Moreover, the incorporation of this polymer into cancer cells induced apoptosis (Figure 1).

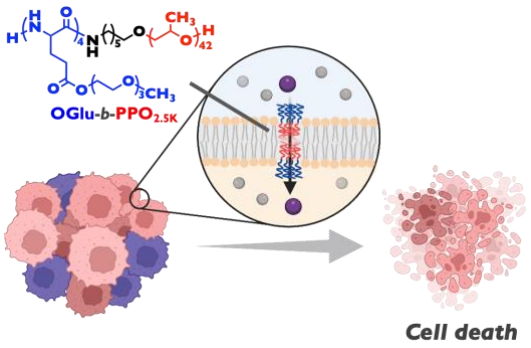

Figure 1: Schematic illustration of OGlu-*b*-$PPO_{2.5K}$ incorporated into cancer cells inducing cell death due to ion permeation.

References

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